IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

IN RE:	
BRIMONIDINE PATENT LITIGATION	MDL Docket No. 07-md-01866 GMS

ALLERGAN, INC'S OPENING MARKMAN BRIEF

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I. INTRODUCTION

The claim construction process in this patent case is very straightforward. The terms of the asserted claims are simple and easy to understand based on their ordinary meaning. Consistent with this, Allergan has proposed constructions in line with established Federal Circuit precedent emphasizing the plain and ordinary meaning considered in light of the patent specifications and file histories, and consistent with this Court's prior construction of the claims.

As further testament to the straightforward nature of the claims of the patents in suit, Allergan and the Apotex defendants (Apotex Corp. and Apotex, Inc.) have agreed that the plain and ordinary meaning controls for every term in each of all five patents-in-suit. There are thus no terms in dispute between Allergan and the Apotex defendants.

By contrast, the Exela defendants (Exela PharmSci, Inc., Exela PharmSci Pvt., Ltd., Paddock Laboratories, Inc., and PharmaForce, Inc.) propose constructions for the '834 patent, the only patent at issue between Allergan and the Exela defendants, that violate numerous claim construction rules. Allergan respectfully requests that the Court adopt the ordinary meaning of the disputed claim terms and adopt the proposed constructions provided in the Revised Joint Claim Chart filed on June 3, 2008.

II. NATURE AND STAGE OF THE PROCEEDINGS AND STATEMENT OF FACTS:

This is Allergan's opening brief in support of its proposed constructions of disputed claim terms. Discovery in this case is underway pursuant to the proposed scheduling order filed and agreed to by the parties. A Markman hearing has been scheduled by the Court for July 16, 2008. Trial is set to commence on March 9, 2009. Relevant facts supporting Allergan's proposed claim constructions are set forth in the Background that follows, as well as in the Argument section.

III. BACKGROUND

A. Allergan's Patents Covering Allergan's ALPHAGAN® P Glaucoma Medication

This case concerns Exela's and Apotex's filings with the United States Food and Drug Administration ("FDA") seeking permission to sell generic formulations of Allergan's highly-successful ALPHAGAN® P 0.15% and 0.1% brimonidine tartrate solution products, which doctors use to treat open-angle glaucoma. In February 2007, Allergan received notification from Exela PharmSci, Inc. that it had filed an Abbreviated New Drug Application ("ANDA") with the FDA for approval of a generic version of ALPHAGAN® P 0.15%.[1] Less than three months later, in May 2007, Allergan received notification from Apotex that it had filed ANDAs for approval of generic versions of both ALPHAGAN® P 0.15% and ALPHAGAN® P 0.1%. All

[1] As jurisdictional discovery in the original California litigation demonstrated, Exela turned out to be a one-man company, with no ability to formulate, manufacture, market, or sell drugs. Instead, Exela markets concepts for potential generic drugs to partners who do the actual work involved. In this case, Paddock Laboratories of Minnesota would be the marketer of the proposed generic Exela product and PharmaForce, Inc. of Ohio would be the manufacturer. [See Appendix at Tab 11, Allergan's Amended Complaint for Patent Infringement filed in *Allergan, Inc. v. Exela PharmSci, Inc., et al.*, CV07-01967 R RCx (C.D. CA. April 26, 2007)] Exela PharmSci Pvt., Ltd. assisted in the development of the generic formulation at issue.

five patents in suit have been asserted against Apotex —United States Patents Nos. 5,424,078 ("the '078 patent"), 6,627,210 ("the '210 patent), 6,637,337 ("the '337 patent"), 6,562,873 ("the '873 patent"), and 6,641,834 ("the '834 patent") [Appendix at Tabs 1 – 5,.[2] while just the '834 patent has been asserted against the Exela defendants.

The Apotex and Exela defendants are not the first companies to attempt to formulate and market a generic version of ALPHAGAN® P 0.15%; Alcon Laboratories, Inc. was the first. Nor is this the first time that litigation involving some of these patents has been before this Court. From 2004 to 2006, this Court presided over litigation, captioned *Allergan, Inc. v. Alcon, Inc.*, No. 04-968 (GMS), which involved Allergan's allegations that Alcon's proposed generic formulation infringed the '834 and '337 patents. That litigation settled on the morning of opening statements for trial. And while the Court is well familiar with the technology at issue in that litigation, we describe it again briefly to refresh the Court's recollection.

B. Brimonidine is a Powerful Glaucoma Medication, First Marketed by Allergan as ALPHAGAN®

Open-angle glaucoma is an incurable disease of the eye that causes gradual vision loss and can lead to blindness. Almost 70 million people worldwide suffer from glaucoma, which is the second leading cause of blindness worldwide. Allergan is a leader in the development of pharmaceutical treatments for glaucoma and invests heavily in research and development related to this chronic ocular disease. Allergan 10-K, 2007 [Appendix Tab 7]

Although there is no cure for the disease, there are various pharmaceutical and surgical treatments that may slow its progression. One of these is to lower the pressure of the fluid in the eye, known as intra-ocular pressure ("IOP"). Scientists and medical personnel believe that the

[2] The intrinsic evidence relied on by the parties, including the patents in suit, can be found in the Appendix that will be filed with the responsive brief as required by the Court's Scheduling Order.

elevated IOP found in glaucoma patients contributes to the gradual retinal deterioration and loss of vision that are characteristics of the disease.

Topically-applied brimonidine, among other things, assists in the lowering of IOP. The drug was originally thought to be merely a blood-pressure medication, but in the early 1990s, Allergan scientists discovered that it was also a powerful medication for lowering IOP. After investing millions of dollars to prove the safety and efficacy of the drug for treatment of open-angle glaucoma, Allergan received approval from the FDA in 1996 and launched its 0.2% brimonidine tartrate ophthalmic solution under the tradename ALPHAGAN®.[3]

ALPHAGAN® 0.2% had a labeled pH range of 5.5 to 6.6. [Appendix Tab 13] ALPHAGAN® 0.2% also contained 0.005% benzalkonium chloride ("BAK") as a preservative. Although ALPHAGAN® 0.2% was very effective at reducing intra-ocular pressure in glaucoma patients, it caused certain undesirable side effects. In particular, approximately 13-16% of patients developed a severe allergy to brimonidine, known as allergic conjunctivitis, that prevented them from being able to use the drug. In addition, the BAK preservative was a known irritant to ocular tissues. Accordingly, at the time the FDA approved the drug, Allergan was already working to improve on ALPHAGAN® 0.2% in the hopes of creating a product with better tolerability that would reduce the side effects.

Today, there are five generic versions of ALPHAGAN® 0.2% available to physicians and patients in the United States. Approved Drug Products with Therapeutic Equivalence Evaluations 28th Edition "The Orange Book", [Appendix Tab 8] Accordingly, there is no barrier to defendants' entering the market for brimonidine tartrate, if they so desire.

[3] Brimonidine is what is known as an "*alpha*-2-adrenergic agonist," hence, the tradename ALPHAGAN®.

C. Allergan's ALPHAGAN® P 0.15% and 0.1% Dramatically Reduce the Problems Associated with ALPHAGAN® 0.2%

The result of Allergan's efforts to develop a product with reduced side effects and a better tolerability profile was ALPHAGAN® P 0.15%. ALPHAGAN® P 0.15% contains 0.15% brimonidine, a twenty-five percent reduction in concentration over the original ALPHAGAN® product. It has a labeled pH range of 6.6-7.4. [Appendix Tab 9] For a preservative, ALPHAGAN® 0.15% contains an oxy-chloro component known as Purite®. [*See* Appendix Tab 9]

ALPHAGAN® P 0.15% was shown in clinical studies to have comparable efficacy to ALPHAGAN® 0.2%, but with a forty-one percent reduction in allergy rate. [Appendix Tab 6, at pages 99-106 of 126] The Purite® preservative used in ALPHAGAN® P 0.15% has also been shown to be far gentler to the eye than the BAK preservative used in ALPHAGAN® 0.2%.

Because of these significant additional patient benefits, Allergan was awarded a three-year market exclusivity period by the FDA for ALPHAGAN® P 0.15%, above and beyond that which Allergan had received for ALPHAGAN® 0.2%. This exclusivity period expired in 2004.

After the FDA approved ALPHAGAN® P 0.15%, Allergan continued its development work to further improve on the product. The result of that work was ALPHAGAN® P 0.1%, which was shown to be just as effective as ALPHAGAN® P 0.15% with a 33% further reduction in the concentration of the brimonidine. ALPHAGAN® P 0.1% has a labeled pH range of 7.4 to 8.0.

Allergan was also awarded a three-year exclusivity for ALPHAGAN® P 0.1%, which expires in August of this year. Allergan currently sells both ALPHAGAN® P 0.15% and ALPHAGAN® P 0.1% formulations for treatment of open-angle glaucoma.

D. The Patents-in-Suit Claim the Inventions that Enabled the Formulation of Brimonidine in the Lowered, More Tolerable Concentration Contained in ALPHAGAN® P

The successful development of the ALPHAGAN® P products hinged on the inventions claimed in the patents-in-suit. As an initial matter, in order to solve the tolerability problem with BAK, researchers employed the Purite® preservative in the formulation, which had been invented by Allergan scientists in the late 1980's. This preservative is covered by the '078 patent.

As for the serious brimonidine allergy problem, researchers concluded that it would be advantageous to formulate the drug in a significantly lower concentration, if efficacy were not compromised. Nonetheless, simply lowering the concentration of brimonidine in the same formulation was not an option, as this would be expected to reduce the drug's effectiveness by a comparable amount.

Through experimentation, Allergan scientists discovered that it was possible to use the desired lower concentration of brimonidine tartrate and maintain effectiveness ***if*** the pH of the formulation was elevated above the pH of the original ALPHAGAN® 0.2% formulation. These higher pH values result in greater concentrations of un-ionized forms of brimonidine. Un-ionized forms of brimonidine diffuse better across the lipid membranes of the eye, making the drug more bioavailable and allowing for use of a lower concentration than in previous drugs. *See* '834 patent, col. 1, lines 34-43, col. 6, lines 8-16. At the lower pHs used in the ALPHAGAN® product, brimonidine is present in a highly ionized form.

Raising the pH of the formulation, however, presented its own set of problems. As the pH increases to the most preferred levels, brimonidine tartrate experiences a rapid drop in solubility. Figure 1 of the patents demonstrates the relationship between solubility and pH. [*See* Appendix Tab 5, at page 2; Tab 3, at page 2] To maintain the advantage of formulating at the

most preferred elevated pHs, Allergan researchers also discovered that it was possible to use components known as solubility enhancing components ("SECs") to increase the solubility of the brimonidine in these solutions. *See, e.g.*, '337 patent, col. 2, lines 9-17.

The '337 and '210 patents claim the use of these solubility-enhancing components ("SECs") with alpha-2-adrenergic agonists such as brimonidine. *See generally* '337 patent, claim 1; '210 patent, claim 1; '873 patent, claim 1. The '337 patent claims the broad category of SECs with alpha-2-adrenergic agonists, while the '210 patent claims more specifically the particular anionic SECs such as carboxymethylcellulose ("CMC") used by Allergan in its ALPHAGAN® P products. *See* '337 patent, col. 6, line 17 to col. 9, line 22; '210 patent at Col. 6, line 32 to col. 9, line 11.

Like the '337 and '210 patent, the '873 patent also claims the use of an SEC with an alpha-2-adrenergic agonist. The claims of the '873 patent, however, also require an oxy-chloro preservative component. The specification of the '873 patent explains that these oxy-chloro preservative components "provide preservative effectiveness, often at a relatively reduced concentration, with little or no detrimental effect on the tissue to which the composition is administered." '873 patent, col. 3, lines 21-25.

As for the '834 patent, that patent generally claims the use of the lowered concentrations of brimonidine at pHs elevated over those used in ALPHAGAN® 0.2%. *See generally* '834 patent, claim 1. As this is the only patent with any terms in dispute, we discuss it in more detail immediately below.

E. The '834 Patent Claims the Use of the Lowered Concentrations of Brimonidine at Elevated pHs.

The '834 patent addresses the inventors' surprising discovery that formulations with a higher pH and substantially lowered concentration of the drug could be made that nonetheless

maintained therapeutic efficacy. The specification explains the inventors' belief that "the un-ionized forms of the adrenergic components facilitate their permeation across membrane lipid bilayers," '834 patent, col. 6, lines 13-16, thus allowing a larger proportion of the adrenergic component to reach the desired site of action. As explained above, the un-ionized form of brimonidine increases quickly as the pH of a brimonidine solution is increased. *See* '834 patent, col. 1, lines 38-41.

The claims of the '834 patent cover this invention. Claim 1 of the '834 patent reads as follows:

> 1. A therapeutically effective aqueous ophthalmic composition comprising:
>
> up to about 0.15% (w/v) of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate, the composition having a pH of about 7.0 or greater, and the 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate being soluble in the composition at about 21° C.

The prosecution of the '834 patent was straightforward. Allergan submitted claims directed to aqueous compositions with up to about 0.15% of active ingredient at a pH of about 7.0 or greater, and the active ingredient being soluble at 21° C. Preliminary Amendment filed 11/01/2002, '834 prosecution history [Appendix Tab 6, at pages 71 - 74 of 126] After the examiner originally rejected these claims as obvious over prior art [*See* Appendix Tab 6, at pages 82 - 83 of 126], Allergan responded to the rejection by submitting a declaration and an article explaining the surprising advantages provided by the 0.15% brimonidine formulation over prior formulations. [*id.*, at pages 91 - 106 of 126] As further explained in the article, the new formulation had the same ability to lower IOP in patients, but resulted a 41% in reduction in allergic conjunctivitis. [*Id.* at 99 of 126][4] The Examiner then allowed the claims.

[4] In addition, Allergan amended the claims to make clear that the invention was directed to therapeutically effective aqueous ophthalmic compositions. [*Id.* at 92 of 126]

IV. DISPUTED TERMS AND THE COURT'S PRIOR CONSTRUCTION OF "ABOUT"

As noted above, there are no terms in dispute for four of the five patents-in-suit: the '078 patent, the '210 patent, the '337 patent and the '873 patent. In addition, Allergan and Apotex agree on the meaning of all terms in the '834 patent.

This leaves only two terms in dispute for the Court to resolve, but only as between Allergan and Apotex on the one hand and Exela on the other. These are:

Term	Allergan's proposed construction	Apotex Defendants' proposed construction	Exela Defendants' proposed construction
"about" as used in the phrase "about 7.0" beginning in Claim 1	approximately	approximately	The therapeutically effective formulation referred to in claim 1 having a pH of 7.0 or greater within measurement tolerances. In no event can the claim cover a formulation having a pH of 6.8 or below.
"A therapeutically effective aqueous ophthalmic composition comprising: up to about 0.15% (w/v) of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate" as used beginning in Claim 1.	The claim requires a therapeutically effective aqueous ophthalmic composition . . . comprising up to approximately 0.15% brimonidine tartrate.	The claim requires a therapeutically effective aqueous ophthalmic composition . . . comprising up to approximately 0.15% brimonidine tartrate.	A water-based formulation containing between 0% and about 0.15% (w/v) of brimonidine tartrate for ophthalmic administration that is demonstrated to provide a therapeutic benefit to a patient to whom the formulation is administered.

The Court reached a construction for the claim term "about" in the prior litigation between Allergan and Alcon, including in the context of pH. Consistent with its plain meaning and case law from the Federal Circuit, the Court construed the term "about" to mean

"approximately." *Allergan, Inc. v. Alcon, Inc.*, No. 04-968 (GMS) (D. Del. July 26, 2005) (Markman Order). The other claim terms raised by Exela have not been considered by the Court before.

V. LEGAL STANDARDS FOR CLAIM CONSTRUCTION

Claim construction is a matter of law exclusively for the Court. *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 391 (1996). The Federal Circuit, following the Supreme Court's opinion in *Markman*, has established numerous principles for ascertaining the proper meaning and scope of patent claims. Those that are currently believed relevant to the disputed terms are discussed below.

A. Claim Terms Are Presumed to Carry Their Ordinary Meaning.

Citing more than a century of Supreme Court precedent, the Federal Circuit very recently reiterated that "[i]t is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Oatey Co. v. IPS Corp.*, 514 F.3d 1271, 1275 (Fed. Cir. 2008), *citing Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005), *citing Innova/PureWater, Inc. v. Safari Water Filtration Systems, Inc.*, 381 F.3d 1111, 1115 (Fed. Cir. 2004). "In construing claims, the analytical focus must begin and remain centered on the language of the claims themselves, for it is that language that the patentee chose to use to 'particularly point[ ] out and distinctly claim[ ] the subject matter which the patentee regards as his invention.'" *Gillette Co. v. Energizer Holdings, Inc.*, 405 F.3d 1367, 1370 (Fed. Cir. 2005), *citing Interactive Gift Express, Inc. v. Compuserve, Inc.*, 256 F.3d 1323, 1331 (Fed. Cir. 2001).

The words used by the patentee to claim his invention are presumed to carry their ordinary and customary meaning. *Phillips*, 415 F.3d at 1313 ("We have frequently stated that the words of a claim 'are generally given their ordinary and customary meaning.'") (quoting

Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996)); *Fuji Photo Film Co., Ltd. v. International Trade Com'n*, 386 F.3d 1095, 1105 (Fed. Cir. 2004) (noting that an accused infringer cannot overcome the heavy presumption that claims should be given their ordinary meaning simply by pointing to the preferred embodiment or other structures or steps disclosed in the specification).

Accordingly, "the claim construction inquiry ... begins and ends in all cases with the actual words of the claim." *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1324 (Fed. Cir. 2002) (quoting *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1248 (Fed. Cir. 1998)). And "[i]n some cases, the ordinary meaning of claim language as understood by a person of skill in the art may be readily apparent even to lay judges, and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words." *Phillips*, 415 F.3d at 1314.

"Dictionaries or comparable sources are often useful to assist in understanding the commonly understood meaning of words and have been used both by our court and the Supreme Court in claim interpretation." *Phillips*, 415 F.3d at 1322. "The ordinary meaning of a claim term may be determined by reviewing a variety of sources, including ... dictionaries and treatises ...." *Teleflex*, 299 F.3d at 1325 (internal citations omitted). "For such ordinary meaning, we turn to the dictionary definition of the term." *Optical Disc Corp. v. Del Mar Avionics*, 208 F.3d 1324, 1334-35 (Fed. Cir. 2000). Although dictionaries technically fall within the category of extrinsic evidence, "judges are free to consult dictionaries and technical treatises 'at any time in order to better understand the underlying technology and may also rely on dictionary definitions when construing claim terms, so long as the dictionary definition does not contradict any definition found in or ascertained by a reading of the patent documents. *Phillips*, 415 F.3d at

1322-23 (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1584 n.6 (Fed. Cir. 1996)). Ultimately, the claim term "is to be given its broadest ordinary meaning consistent with the written description." *Int'l Rectifier Corp. v. IXYS Corp.*, 361 F.3d 1363, 1373 (Fed. Cir. 2004).

B. The Scope of a Claim Term May Not Be Limited by Reading in Limitations from the Specification.

It is a "cardinal sin" to read a limitation from the written description into the claims. *Phillips*, 415 F.3d at 1320; *SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1341 (Fed. Cir. 2001). The rule against importing limitations into claims is succinctly explained as follows: "[i]f everything in the specification were required to be read into the claims, or if structural claims were to be limited to devices operated precisely as a specification-described embodiment is operated, there would be no need for claims." *SRI Int'l v. Matsushita Elec. Corp. of Am.*, 775 F.2d 1107, 1121 (Fed. Cir. 1985). Patentees are not required to include within each of their claims all of the advantages or features described as significant or important in the written description. *Golight, Inc. v. Wal-Mart Stores, Inc.*, 355 F.3d 1327, 1331-1332 (Fed. Cir. 2004). This must be the case because "[a]n invention may possess a number of advantages or purposes, and there is no requirement that every claim directed to that invention be limited to encompass all of them." *E-Pass Techs., Inc. v. 3Com Corp.*, 343 F.3d 1364, 1370 (Fed. Cir. 2003). Similarly, "[a]n applicant is not necessarily required by 35 U.S.C. § 112, ¶ 1, to describe more embodiments than its preferred one, and [the Federal Circuit has] outright rejected the notion that disclosure of a single embodiment necessarily limits the claims." *Golight*, 355 F.3d at 1332; *see also Phillips*, 415 F.3d at 1323 ("[W]e have expressly rejected the contention that if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment."); *Teleflex*, 299 F.3d at 1327 (stating that "the

number of embodiments disclosed in the specification is not determinative of the meaning of disputed claim terms"). Thus, "particular embodiments appearing in the written description will not be used to limit claim language that has broader effect." *Innova*, 381 F.3d at 1117.

C. Any Alleged Disavowal of the Ordinary Meaning from the Prosecution History or Patent Specification Must be Clear and Unequivocal.

Regardless of the number or ways or detail with which features are described in the written description, the Federal Circuit has circumscribed the ways in which a court may constrict the ordinary meaning of a claim term, based on either the patent specification or prosecution history. As to the specification, the written description may only be used to restrict the scope of the claims if "the patentee demonstrated an intent to deviate from the ordinary and accustomed meaning of a claim term by redefining the term or by characterizing the invention in the intrinsic record using words or expressions of manifest exclusion or restriction, representing a clear disavowal of claim scope." *Teleflex*, 299 F.3d at 1327; *see also Phillips*, 415 F.3d at 1314 ("[T]he specification may reveal an intentional disclaimer, or disavowal, of claim scope by the inventor. In that instance . . . the inventor has dictated the correct claim scope, and the inventor's intention, as expressed in the specification, is regarded as dispositive."). The patent's written description may not be used to narrow the scope of the claimed invention absent a clear disclaimer. *Brookhill-Wilk 1, LLC v. Intuitive Surgical, Inc.*, 334 F.3d 1294, 1301 (Fed. Cir. 2003) ("Absent a clear disclaimer of particular subject matter, the fact that the inventor anticipated that the invention may be used in a particular manner does not limit the scope to that narrow context."). In short, the presumption in favor of the broad construction of a claim term will only be overcome where the patentee, acting as his or her own lexicographer, has clearly set forth an explicit definition of the term different from its ordinary meaning. *See In re Paulsen*, 30

F.3d 1475, 1480 (Fed. Cir. 1994); *Intellicall, Inc. v. Phonometrics, Inc.*, 952 F.2d 1384, 1387-88 (Fed. Cir. 1992).

As to the prosecution history, the Federal Circuit has consistently declined to find any disclaimer based on prosecution history unless the alleged disavowal of claim scope is "clear and unmistakable." *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1325-26 (Fed. Cir. 2003); see also Phillips, 415 F.3d at 1317 ("because the prosecution history represents an ongoing negotiation between the PTO and the applicant, rather than the final product of that negotiation, it often lacks the clarity of the specification and thus is less useful for claim construction purposes.") If the disclaimer is ambiguous, disavowal will not be found. *Id.* ("We have, however, declined to apply the doctrine of prosecution disclaimer where the alleged disavowal of claim scope is ambiguous."); *N. Telecom Ltd. v. Samsung Elecs. Co.*, 215 F.3d 1281, 1293-95 (Fed. Cir. 2000) (refusing to limit scope of claims where inventors' statements were amenable to multiple reasonable interpretations); *Rexnord*, 274 F.3d 1336, 1347 (refusing to limit the ordinary meaning of the claim because the alleged disclaimer in the file wrapper was at best "inconclusive").

D. Extrinsic Evidence Should Not be Used to Alter the Claim's Meaning

Under the Federal Circuit's current guidelines, extrinsic evidence continues to play a limited role in the claim construction process. *Phillips*, 415 F.3d at 1320-1321; *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1583 (Fed. Cir. 1996). While a court may accept extrinsic evidence to explain the technology, a court should not employ such evidence to interpret the claim terms where their meaning is clear from the intrinsic sources. *See Playtex Prods., Inc. v. Procter & Gamble Co.*, 400 F.3d 901, 907-08 (Fed. Cir. 2005).

VI. ARGUMENT

Based on these legal standards, the disputed claim limitations should be interpreted consistent with their ordinary meaning, as proposed by Allergan. The disputed (and non-disputed) terms in the asserted claims are all straightforward and require nothing more in the way of claim construction other than confirming their ordinary meaning, a position with which Apotex agrees.

A. "About" Should be Construed Consistent with its Adjudicated Ordinary Meaning as "Approximately"

> 1. A therapeutically effective aqueous ophthalmic composition comprising:
> up to about 0.15% (w/v) of a component selected from 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate, the composition having a pH of *about 7.0* or greater, and the component being soluble in the composition at about 21° C.
>
> 10. A therapeutically effective aqueous ophthalmic composition comprising:
> up to about 0.15% (w/v) of a component selected from 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline, salts of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline, esters of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline and mixtures thereof, the composition having a pH of *about 7.0* or greater, and the component being soluble in the composition at about 21° C.

As repeatedly adjudicated by the Federal Circuit, the ordinary meaning of "about" is "approximately." *See Merck & Co. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1369-70 (Fed. Cir. 2005) (holding that the ordinary meaning of "about" is "approximately"). *See also Conopco, Inc. v. May Dep't Stores Co.*, 46 F.3d 1556, 1561 n.2 (Fed. Cir. 1994) (noting that ordinary meaning of "about" is approximately). This is also the dictionary definition of the term *See Webster's Third New International Dictionary* 5 (1993) (defining "about" as "with some approach to exactness in quantity, number, or time: approximately") [Appendix Tab 14].

Apotex and Allergan agree on this definition. As for the Exela defendants, they offer the Court conflicting positions on the term. While, on the one hand Exela disputes the meaning of the term "about" in the limitation requiring that the composition has a pH of "about 7.0 or

greater," asserting that the claim "cannot cover a formulation having a pH of 6.8 or below," as in claims 1 and 10 of the '834 patent, on the other hand, Exela acknowledges that "about" means "approximately," as in claims 3 and 12 of the '834 patent. [Joint Claim Chart.]

Under Allergan's and Apotex's proposed construction, the term "about" carries its adjudicated ordinary meaning of "approximately" in *all* its usages in the '834 patent claims. This, too, is consistent with Federal Circuit precedent. *Rexnord Corp. v. Laitram Corp.*, 274 F.3d 1336, 1342 (Fed. Cir. 2001) (holding that "a claim term should be construed consistently with its appearance in other places in the same claim or in other claims of the same patent").

Allergan and Apotex's position with respect to the term "about" is also consistent with the position taken by Allergan in the *Allergan, Inc. v. Alcon, Inc.*, No. 04-968 (GMS), litigation before this Court concerning the '834 patent. There, Alcon attempted to impose artificial limitations on the term "about" that were inconsistent with the ordinary meaning, but the Court agreed with Allergan that the ordinary meaning of "approximately" should apply. *Allergan, Inc. v. Alcon, Inc.*, No. 04-968 (GMS) (D. Del. July 26, 2005) (Markman Order).

Other district courts have also followed the precedent set forth in *Merck*. *See, e.g.*, *Biopolymer Eng'g, Inc. v. Immunocorp*, Nos. 05-536, -2972, 2007 WL 4562592, at *12 (D. Minn. Dec. 21, 2007) (construing 'about' as 'approximately' in four separate claim constructions, citing *Merck* and noting that "the Court declines to arbitrarily construe 'about' through use of rounding principles" but "gives the term 'about' its ordinary meaning of 'approximately'"); *Amazin' Raisins Int'l, Inc. v. Ocean Spray Cranberries, Inc.*, No. 04-12679, 2007 WL 2386360, at *12 (D. Mass. Aug. 20, 2007) ("[U]nless the patentee serves as his own lexicographer and defines the term ['about'] differently, it should be given its ordinary and accustomed meaning of 'approximately.'"); *Novartis Pharm. Corp. v. Apotex Corp.*, No. 02-

8917, 2006 WL 626058 at *10 (S.D.N.Y. Mar. 13, 2006) ("I find that the term 'about' should be construed to mean 'approximately.'") (citing *Merck*)).

The specification of the '834 patent is entirely consistent with this ordinary meaning of the term "about," and there is nothing to indicate that the term should be interpreted differently for its use in the pH limitation (as opposed to the temperature and concentration limitations) or that it should somehow exclude a pH of 6.8 or lower, as Exela suggests. The specification repeatedly refers to the pH of the formulation in approximate terms, for example, explaining that the carrier has a pH of "about 6 to about 9 or about 10, more preferably about 6 to about 8, and still more preferably about 7.5." *See* '834 patent, col. 11, lines 3-6. Example 2 of the patent also refers to measuring the pH "from about 7 to about 10," where the pH measurements were actually taken over a range of 6.67 up to 10.11. *Id.* at col. 15, lines 23-24 (discussing Table 4). Indeed, the table setting forth this example includes multiple data points with pHs below 7.0, including 6.67, 6.68 and 6.93. [*Id.* at Table IV] This, alone, demonstrates the erroneous nature of Exela's proposed construction, as the specification explicitly includes pHs – 6.67 and 6.68 – that Exela's construction would exclude.

Accordingly, Exela's proposed construction ignores the broad ordinary meaning of "about," and instead attempts to impose an artificial limit on the term. It is also plainly inconsistent with the specification's description of the scope of the term "about" as it relates to pH. The Court should once again apply the adjudicated meaning of the term "about", which is "approximately."

B. "Therapeutically Effective" Should be Construed in Accordance With its Plain Meaning.

1. A *therapeutically effective aqueous ophthalmic composition* comprising: up to about 0.15% (w/v) of a component selected from 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate, the composition having a pH of about 7.0 or greater, and the component being soluble in the composition at about 21° C.

> 10. A *therapeutically effective aqueous ophthalmic composition* comprising: up to about 0.15% (w/v) of a component selected from the group consisting of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline, salts of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline, esters of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline and mixtures thereof , the composition having a pH of about 7.0 or greater, and the component being soluble in the composition at about 21° C.

Consistent with the plain and ordinary meaning of the phrase, Allergan's and Apotex's construction for "therapeutically effective" means just that, "therapeutically effective." The Exela defendants, on the other hand, have proposed a construction that seeks to unnecessarily reword the limitation. According to the Exela defendants, the limitation requires that the formulation "is demonstrated to provide a therapeutic benefit to a patient to whom the formulation is administered." Exela's motivation in rewording the claim language—which is already plain on its face—is unclear. There is no need to construe this limitation in any way other than as it is written because the "therapeutically effective" term, a commonly used term in pharmaceutical patents, is clear on its face. *See e.g., Board of Trustees of Leland Stanford Junior University v. Roche Molecular Systems, Inc.*, 528 F.Supp.2d 967, 976-77 (N.D. Cal. 2007) ("The terms 'therapeutically effective' or 'therapeutically ineffective' are commonplace-a juror can easily use these terms in her infringement fact-finding without further direction from the court. . . . These terms do not need to be construed because they are neither unfamiliar to the jury, confusing to the jury, nor affected by the specification or prosecution history.)

The construction proposed by Allergan and Apotex is more consistent with the plain meaning of the claims, and the Court should therefore construe the term as Allergan requests and reject the proposed construction of the Exela defendants.

VII. CONCLUSION

For all the reasons stated above, and those to be stated in later briefing and at argument, Allergan respectfully requests that its proposed claim constructions be adopted.

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CERTIFICATE OF SERVICE

I hereby certify that on June 3, 2008, I electronically filed with the Clerk of Court Allergan, Inc.'s Opening Markman Brief using CM/ECF which will send electronic notification of such filing(s) to the following Delaware counsel. In addition, the filing will also be sent via hand delivery:

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